

**REMARKS*****Status of the claims***

Claims 9, 10, 13-15, and 23-39 were pending in this application. Claims 10, 13, and 14 were previously withdrawn from consideration as drawn to a non-elected invention. Claims 9, 24, 27, 34, 36, and 38 have been amended herein. Claims 9, 15, and 23-39 are currently under consideration.

The amendments to claims 9 are supported in the specification, for example, in Example 1. The amendments to claims 24, 27, 28, 34, 35, 36, and 38 were made to for clarity, to correct clerical and/or typographical errors, and/or to amend claim dependency. No new matter has been added by the foregoing amendments.

With respect to claim amendments and canceled claims, Applicants have not dedicated to the public or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

***Information Disclosure Statement***

An Information Disclosure Statement is filed concurrently herewith. Applicants would appreciate the Examiner initialing the Form SB/08 a/b, indicating that the references listed therein have been considered and made of record in this application.

***Sequence Compliance***

In response to the Notice to Comply, a substitute sequence listing is filed herewith, identifying nucleotide sequences disclosed in the specification with Sequence Identification Numbers. The specification and drawings have also been amended accordingly herein.

***Rejections under 35 U.S.C. §102(b)***

Claims 9, 24-27, 29, and 38 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Zubiaga et al. (1995) *Molecular and Cellular Biology* 15(4):2219-30 ("Zubiaga"). Applicants respectfully traverse this rejection.

The present claims as amended are drawn to a transfected cell line comprising a DNA expression vector encoding a first protein having a detectable signal and a control expression vector encoding a second protein having a detectable signal. Both the expression vector and the control vector comprise one or more 3'UTR sequence and one or more expression control sequence operatively associated with the DNA sequence that encodes a detectable protein, *wherein the 3'UTR sequences in the expression vector and the control vector are derived from the same gene*. The expression vector also contains a heterologous instability sequence DNA. Since the 3'UTR sequences are from the same gene, a comparison may be made between expression of reporter genes in the presence and absence of the instability sequence without the additional variable of differing UTR sequences from different genes.

In contrast, Zubiaga discloses expression vectors that express  $\beta$ -globin mRNA, with a *c-fos* promoter and variants of the *c-fos* AU-rich mRNA instability sequence inserted into the  $\beta$ -globin 3'UTR. Zubiaga discloses transient co-transfection of the  $\beta$ -globin construct and a control vector that constitutively expresses *lacZ* mRNA, into NIH 3T3 fibroblasts. The  $\beta$ -globin construct and the *lacZ* construct have 3'UTR sequences derived from different genes, and thus this reference does not anticipate the claimed invention which requires that expression and control vector 3'UTR sequences be derived from the same gene.

Further, the present claims recite both an expression vector and a control vector that each encode a protein having a detectable signal. The  $\beta$ -globin construct of Zubiaga does not encode a protein having a detectable signal.  $\beta$ -globin mRNA is detected in Zubiaga by Northern blot, not by a detectable signal produced by the protein.  $\beta$ -globin does not produce a detectable signal, as required by the claimed invention.

Zubiaga does not teach either expression and control vectors with 3'UTR sequences from the same gene or an expression vector that encodes a protein having a detectable signal and thus does not anticipate the claimed invention.

With regard to the rejection of claim 25, Applicants note that the ARE variant sequences inserted in 3'UTR of the  $\beta$ -globin construct of Zubiaga do not contain sequences that flank the mRNA instability sequence in the naturally-occurring gene (*i.e.*, *c-fos*) from which the instability sequence is derived, as required by this claim.

With regard to the rejection of claim 27, Applicants note that the ARE variant sequences in the  $\beta$ -globin construct of Zubiaga do not comprise DNA comprising the whole or a substantial part of the 3'UTR from the naturally occurring (*i.e.*, *c-fos*) gene, as required by this claim.

With regard to the rejection of claim 38, Applicants note that this claim is dependent on claim 30, which is directed to a set of transfected cell lines, comprising a cell line comprising a DNA expression vector and a cell line comprising a control vector. Zubiaga does not disclose expression and control vectors in separate cell lines, as required by claim 38.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b).

Claims 30-34, 36, 37, and 39 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Banholzer et al. (1997) *Molecular and Cellular Biology* 17(6):3254-60 ("Banholzer"). Applicants respectfully traverse this rejection.

The present claims as amended are drawn to a set of transfected cell lines comprising a transfected cell line comprising a DNA expression vector encoding a first protein having a

detectable signal and a transfected cell line comprising a control expression vector encoding a second protein having a detectable signal. The expression vector contains a heterologous instability sequence DNA.

In contrast, Banholzer discloses constructs comprising the 3'UTR of IL-3, either with or without the 3' ARE-containing sequences. These constructs contain either the wild-type 3'UTR sequence of IL-3, or a wild-type UTR from which the native instability sequence is absent. The constructs of Banholzer do not contain an instability sequence from a heterologous instability sequence DNA, as required by the instant claims. Banholzer discloses presence or absence of an instability sequence, not addition of a heterologous instability sequence as claimed. Banholzer does not teach a construct comprising an instability sequence DNA that is heterologous to 3'UTR of the construct and does not anticipate the present claims which require such a heterologous instability sequence.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b).

***Rejections under 35 U.S.C. §103(a)***

Claims 15 and 23 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Zubiaga, in view of Banholzer. Applicants respectfully traverse this rejection.

As discussed above, Zubiaga does not teach a single cell line comprising both expression and control vectors with the same 3'UTR sequences, wherein the expression vector comprises a heterologous mRNA instability sequence. Zubiaga also does not teach a single stably transfected cell line comprising both of these vectors. Banholzer does not cure the deficiencies of Zubiaga.

A *prima facie* case for obviousness requires, *inter alia*, that references when combined must teach or suggest all of the elements of a claimed invention. Banholzer does not teach or suggest incorporating expression and control vectors as claimed into a single stably transfected cell line. The vectors of Banholzer are transfected into separate cell lines and are tested in separate cell lines. There is no teaching or suggestion in Banholzer that incorporation of expression and control

vectors into single cell line would be advantageous. As discussed above, Banholzer does not teach an expression vector into which a heterologous instability sequence has been introduced, and thus further does not provide a suggestion to produce the claimed cell line which contains such a sequence.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a).

Claims 28 and 35 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Zubiaga or Banholzer, in view of Lemm and Ross (2002) *Molecular and Cellular Biology* 22(12):3959-69. Applicants respectfully traverse this rejection.

As discussed above, Zubiaga does not teach a transfected cell line comprising both expression and control vectors with the same 3'UTR sequences, wherein the expression vector comprises a heterologous mRNA instability sequence. Lemm and Ross does not cure this deficiency. Lemm and Ross describe a *c-myc* CRD sequence, but do not describe or suggest a cell line that comprises both expression and control vectors as claimed. Thus, the combination of these references fails to teach or suggest all of the elements of claim 28, as required for a *prima facie* case for obviousness.

As discussed above, Banholzer does not teach an expression construct comprising an instability sequence DNA that is heterologous to the 3'UTR of the construct. Lemm and Ross also do not teach or suggest such a construct. Thus, the combination of these references fails to teach or suggest all of the elements of claim 35, as required for a *prima facie* case for obviousness.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a).

***Rejections under 35 U.S.C. § 112, second paragraph***

Claims 9 and 30 are rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite due to recitation of “a second DNA sequence corresponding to one or more mRNA instability sequence derived from . . .” Applicants respectfully traverse this rejection.

The Examiner states that the scope of the term “corresponding” is unclear with respect to whether it means that the DNA shares homology or comprises the mRNA instability sequence. Applicants respectfully disagree that this term is unclear. The specification states on page 11 that the terms “‘corresponds to’ and ‘corresponding to’ are used . . . to describe the relationship between a DNA sequence and a RNA sequence wherein the DNA sequence is the direct counterpart of the RNA sequence and vice versa, i.e. the two sequences are identical with the exception that when a ‘T’ base occurs in a DNA sequence it is replaced with a ‘U’ base in the RNA counterpart sequence.” Thus, this terminology has been explained in the specification as filed, and Applicants respectfully submit that the claims are clear as written.

The Examiner also states that the term “derived” renders the claims indefinite “because the nature and number of derivative process is unknown.” Applicants respectfully disagree that this term renders the claims indefinite. The plain meaning of the term “derive” is “to take, receive, or obtain especially from a specified source.” Merriam-Webster Dictionary, 2007. The claims recite “one or more mRNA instability sequence *derived* from one or more naturally occurring genes.” In this context, “derived” indicates that the source from which the one or more mRNA instability sequence in the expression vector is obtained is one or more naturally occurring genes. The usage of this term is in accordance with the dictionary definition for “derive.” Thus, Applicants respectfully submit that this term is not indefinite and the claims are clear as written.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

Claim 38 is rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite due to recitation of the phrase “wherein said heterologous instability sequence in said transfected cell

line comprising a DNA expression vector is inserted into said 3'UTR sequence." The Examiner states that "it is unclear whether it is the instability sequence of the expression vector . . . inserted into said 3'UTR." Claim 38 has been amended herein to recite "wherein said heterologous instability sequence is inserted into said 3'UTR sequence in said DNA expression vector," solely to clarify the claim.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

### CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 608352000100. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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